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Tahrani, Abd A.

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Ethnic Differences In The Pathogenesis of Obstructive Sleep Apnoea: Exploring Non-Anatomical Factors

Abd A Tahrani

Institute of Metabolism and Systems Research, University of Birmingham, UK.

Centre of Endocrinology, Diabetes and Metabolism, Birmingham Health Partners, Birmingham, UK

Department of Diabetes and Endocrinology, Birmingham Heartlands Hospital, Birmingham, UK

Corresponding author:

Abd A Tahrani

Department of Diabetes and Endocrinology,

Birmingham Heartlands Hospital,

Birmingham B9 5SS

07801549960

a.a.tahrani@bham.ac.uk or abd.tahrani@nhs.net

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Obstructive sleep apnoea (OSA) is a common disorder that affects 17-26% of men and 9-28% of women[1]. The instability and increased collapsibility of the upper airways during sleep are the cardinal features of OSA, which result in recurrent upper airway obstruction resulting in either complete or partial cessation of airflow that leads to the characteristic features of OSA such as recurrent oxygen desaturations, disruption of sleep architecture and cyclical changes in heart rate, blood pressure and sympathetic activity[2].

Considering that obesity is a major risk factor of OSA, it is not surprising that the prevalence of OSA increases with increasing prevalence of obesity[3]. OSA prevalence and severity have been shown to increase with weight gain and improve with weight loss[4;5]. In addition to obesity, craniofacial features and surface anatomy (such as cervicomental angle and face width) and upper airway structures (such as tongue volume and soft palate length) are associated with OSA[6-8]. Furthermore, a crowded posterior oropharynx and a steep thyromental plane are associated with OSA in Asian and White patients independently of obesity[9].

In addition to obesity and craniofacial anatomy, other non-anatomical factors such as low arousal thresholds (ArTH), passive critical closing pressure of the upper airway, loop gain, and upper airway muscle responsiveness play an important role in the pathogenesis of OSA[10]. The upper airway obstruction that occurs in OSA leads to an increase in CO_2 levels that leads to increased ventilatory drive and increasingly negative pharyngeal pressure which in turn can activate the upper airway dilator muscles to open the obstructed upper airway and restores its patency[11]. However, early arousals due to low ArTH can interrupt this process and result in restoration of upper airway patency before the development of adequate ventilatory drive, which can lead to further multiple upper airway obstructions[11]. A low respiratory ArTH is present in a third of patients with OSA[11].

Studies that examine ethnic differences in OSA prevalence show inconsistent results[12-14]. However, several studies have shown that Asian patients have similar OSA prevalence to that reported in studies conducted in Europe and North America. This is despite the fact that Asians were less obese

(based on body mass index (BMI))[15]. In addition, the OSA phenotype differs amongst ethnicities, which can partly be explained by differences in obesity and craniofacial anatomy. Our group has shown that differences in adiposity, particularly upper body fat distribution, may explain our findings of a higher prevalence of OSA in White Europeans vs. South Asians with Type 2 diabetes[16]. Another study found that the contribution of obesity and craniofacial features to OSA differed between Caucasians and Chinese patients with similar OSA severity- the Caucasians were more obese while the Chinese exhibited more craniofacial restriction[17;18]. However, whether non-anatomical factors contribute to the ethnic differences in OSA phenotype has not previously been studied.

In this issue of *Respirology* Lee at al. provide evidence that non-anatomical factors contributing to the pathogenesis of OSA differ significantly between White Caucasians and Chinese with moderate to severe OSA (based on polysomnography). This study shows that a low respiratory ArTH is significantly less common in Chinese patients with moderate to severe OSA compared to White Caucasians and that the ArTH was less negative in Caucasians compared to Chinese with moderate to severe OSA[19]. Low respiratory ArTH in this study was defined as having at least two of the following criteria: apnoea hypopnea index < 30/hour, nadir oxygen saturation > 82.5%, and percentage of hypopneas out of the total respiratory events > 58.3%[19]. This scoring system was validated to predict a low ArTH (defined as overall ArTH less negative than −15 cmH2O on epiglottic pressure catheter) by Bradley et al.; a score of 2 or more had correctly predicted a low ArTH in 84.1% of cases with a sensitivity, a specificity, a positive predictive value and a negative predictive value all over 80%[11]. In addition, and after considering craniofacial anatomy, the proportion of White Caucasians with moderate to severe OSA who had low respiratory ArTH was lower in those who had severe craniofacial anatomical compromise; While in the Chinese patients with moderate to severe OSA there was no such differences in the prevalence of low respiratory ArTH between those with and without craniofacial anatomical compromise[19]. In a sub-group analysis in which the White Caucasian and Chinese patients with moderate-severe OSA were matched for BMI; OSA was more

severe in the Chinese patients and the ArTH was less negative in the White Caucasians. However, matching for BMI does not necessary reflect matching for adiposity as Asians are known to have higher visceral adiposity compared to White Caucasians with similar BMI[20]. This might explain the higher prevalence of OSA in the Chinese patients compared to the White Caucasians with similar BMI in this subgroup analysis. It must be noted that the criteria used for assessing low ArTH in this study were validated previously in White Caucasian populations and not in Chinese population[11].

This study suggests that OSA in Chinese patients is more driven by anatomical factors while in White Caucasians non-anatomical factors play a more important role. This is relevant when considering individualising screening and treatment strategies for patients with OSA. For example, treatments aimed at improving low respiratory ArTH may only be beneficial in patients who have low respiratory ArTH as part of the pathogenesis of their OSA, while in other patients such treatment may have no impact or even a detrimental effect on AHI[21;22].

In conclusion, the current study by Lee et al suggests that there are ethnic differences in the pathogenesis of OSA between Chinese and White Caucasians with moderate to severe OSA. The authors demonstrate that the contributions of obesity, craniofacial anatomy and respiratory ArTH to OSA pathogenesis differs between White Caucasians and Chinese patients with moderate to severe OSA. Further research exploring ethnic differences in OSA pathogenesis is needed in order to individualise treatment and screening strategies.

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